REMARKS

Entry of the foregoing amendments and reconsideration of the claims of the subject application, in light of the following remarks, is respectfully requested.

Claims 35 and 62 have been cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Applicants have amended claims 1, 19, 25, 32, 38, 39, 42, 50, 52, 53, 54, 63, 64, 71, 74, 82, 96, 100, and 122. Claims 1-19, 25, 38, 39-42, 50, 63-64, 71, 74, 82, 96, 100 and 122 have been amended to clarify the claimed subject matter. Support for this amendment to the claims may be found, at the very least, on page 27, lines 28-30; in Example 5, page 86, line 12, to page 88, line 37, of the specification as filed. Claims 52, 53 and 54 have been amended to include the FR consensus sequence in the heavy and light chain variable domains. Support for this amendment to claims 52-54 may be found, at the very least, on page 41, lines 6-15. No new matter enters by way of this amendment.

Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 1-74 and 82-127 are rejected under 35 U.S.C. § 12, first paragraph, for an alleged lack of written description. The Examiner has several basis for the rejection including: 1) the structure of the antibody such as amino acid sequence; 2) whether the FR is from heavy or light chain; 3) the type of amino acids to be substituted; and 4) the position or location of amino acids in the FR or mixture of FR. Applicants traverse this rejection.

The Examiner continues to assert that the specification does not provide written description support for methods of producing any antibody or antigen binding fragment in high yield from a host cell. According to the Examiner, the specification only provides adequate written description support for methods of producing anti-VEGF antibodies or antigen binding fragments thereof in high yield. Applicants respectfully disagree.

As was noted previously, there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed, 66(4) *Fed Reg.* 1099, 1105 (2001); *see also*, *In re Wertheim*, 191 USPQ 90, 97 (CCPA 1976). Compliance with

the written description requirement does not require an applicant to describe exactly the subject matter claimed; rather, the description must clearly allow a person of ordinary skill in the art to recognize that he or she invented what is claimed. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Furthermore, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by reduction to practice, by disclosure of relevant identifying characteristics such as structure, physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of these characteristics. *MPEP 2163 II. A.3.(a)ii)*. The test is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that applicant had possession of the subject matter later claimed. *In re Kaslow*, 217 USPQ 1089 (Fed. Cir. 1991).

The specification clearly provides an adequate written description of the claimed methods. The Examiner appears to agree with this, as she admits that at the specification discloses methods of producing anti-VEGF antibodies or antigen binding fragment in high yield (see the paragraph bridging pages 4 and 5 of the Office Action mailed December 18, 2006). However, Applicants submit the specification describes production of any antibody. "An applicant is not required to describe in the specification every conceivable and possible future embodiment of his invention." *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1344 (Fed. Cir. 2001). "A specification may, within the meaning of 35 U.S.C. § 112 para. 1, contain a written description of a broadly claimed invention without describing all species that [the] claim encompasses." *Utter v. Hiraga*, 845 F.2d 993, 998 (Fed. Cir. 1988).

In the present case, the specification broadly describes methods of producing antibodies or antigen binding fragments in high yield from a host cell. In support of the methods, Applicants also provide examples where the methods are used to produce anti-VEGF antibodies in high yield. However, Applicants describe using these same methods to produce antibodies to other proteins in high yield. *See* page 4, lines 3-10, of the specification as filed. Each of the steps used to modify the VEGF antibody can be used to modify any antibody. Again, the test is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that applicant had possession of the subject matter later claimed. *In re Kaslow*, 217

USPQ 1089 (Fed. Cir. 1991). The specification does convey that the Applicants had possession of methods to modify any antibody to produce such antibodies in high yield, and "possession of the subject matter" does not require actual reduction to practice of each and every possible embodiment.

The Examiner contends that the specification fails to describe the amino acid sequence and structure of antibodies or antibody fragments. Applicants respectfully disagree. Applicants have described antibodies, antibody variable regions, hypervariable regions, and framework regions at page 16, line 9 to page 22, line 22. Applicants have exemplified the methods as claimed with several different anti-VEGF antibodies and anti-IgE antibodies and provided the sequences at Figures 15-23. The structure and sequence of any antibody may be known or readily obtainable. Antibody variable domain structure is known and sequences can be readily obtained. The human subgroup consensus sequences are also known and available from publicly available sources. Thus, Applicants submit that the specification describes not only antibody structures and sequences, but such sequences are known to those of ordinary skill in the art.

The Examiner also contends that the specification does not describe which framework of which heavy or light chain is to be modified. Applicants submit that Applicants have described modifications to both heavy and/or light chain variable domains, at least at page 33, line 1 to page 35, line 31 in the specification. Applicants have exemplified modifications to FR1, FR2, FR3 of the heavy chain in Figure 13 and Example 7. Applicants have also exemplified changes to light chains FR1 and FR3 in Example 6 and Figures 8-10. Applicants have shown that the methods as claimed can be applied to any FR region of the light and/or heavy chain variable domain. The Examiner has presented no technical or scientific reasoning as to why the claimed methods would not work with any antibody or antibody framework region to be modified. Thus, Applicants submit that one of ordinary skill in the art would understand Applicants were in possession of the claimed subject matter.

The Examiner also contends that Applicants do not describe the type of amino acids to be substituted. Applicants respectfully disagree. Applicants submit that the FR of the antibody or antibody fragment is compared to the selected FR consensus sequence. These consensus sequences are known or can be readily determined. The amino acid positions and amino acids to

be substituted are determined by aligning the FR to be modified with the sequence of the selected consensus subgroup sequence, and at least one amino acid position that differs in the antibody or antibody variable domain is substituted with the amino acid at that position in the selected subgroup consensus sequence as described and exemplified in the specification at least at page 36, line 7 to page 37, line 24. The Examiner contends that position or location of amino acids with the FR or mixture of FRs is not described. As described above, Applicants have described and exemplified the location of the amino acid positions to be modified. In addition, Applicants have described how for any FR, one of skill in the art can determine which amino acid positions can be substituted in the least at page 68, line 10 to page 70, line 25. Applicants have also exemplified that modification to at least FR1, FR2, and FR3 can improve yield. There is no reason to believe that the same methods can be applied to FR4 with similar results. The Examiner has presented no technical or logical reason why the same methods can be applied to FR4 as well as FR1, FR2 and/or FR3.

Finally, with respect to claims 52-54, these claims have been amended to recite that the antibody or antigen binding fragment has the light chain framework regions from the human light chain variable domain Kappa subgroup I consensus sequence (see claims 52 and 54) or that the antibody or antigen binding fragment has the heavy chain framework regions from the human heavy chain variable domain subgroup III consensus sequence (see claims 53 and 54). See page 41, lines 6-15, of the specification as filed. With respect to claims 56 and 56, as mentioned on page 41, lines 16-22, the cys residues that form the intrachain disulfide bond in a variable domain are usually at conserved positions. Thus, the amino acid positions adjacent to the cys residues in the heavy chain variable domain (amino acid positions 20, 21, 23, 24, 90, 91, 93 and 94) and in the light chain variable domain (amino acid positions 21, 22, 24, 25, 86, 87, 89 and 90) are conserved.

It is thus clear that the specification reasonably conveys to a person having ordinary skill in the art that the Applicants had possession of methods of modifying any antibody to produce the antibodies in high yield. Therefore, withdrawal of this rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejection of Claims 1-74 and 82-127 Under 35 U.S.C. § 112, Second Paragraph

Claims 1-74 and 82-127 have been rejected under 35 U.S.C. § 112, second paragraph, for purportedly being indefinite. For at least all of the reasons set forth below, withdrawal of this rejection is believed to be in order.

Claims 1-74 and 82-127 have been rejected under 35 U.S.C. § 112, second paragraph, for purportedly omitting essential steps. In order to expedite prosecution, and in no way acquiescing to the correctness of the rejection, the claims have been amended to include the step of aligning the HVR1 and/or HVR2 regions of the non-human antibody to the corresponding HVR1 and/or HVR2 sequences of the human subgroup consensus sequences.

Claims 1, 25, 39, 50, 74, 82, 96, 100 and 104 have been rejected under 35 U.S.C. § 112, second paragraph, for purportedly failing to achieve the goal set forth in the preamble. While not acquiescing to the rejection and solely to expedite prosecution, claims 1, 50, 74, 82, 96 and 100 have been amended to indicate that the modified antibodies or fragments thereof have improved yield, thereby rendering their rejection moot. Claim 25 is not directed to a method of improving the yield of an antibody, and therefore amendment is not necessary. Claims 39 and 104 already include that the yield is improved, and therefore further amendment is not necessary.

Claims 35 and 62 are purportedly indefinite, for failing to further limit the claim from which they depend. While not acquiescing to the rejection and solely to expedite prosecution, claims 25 and 50 now indicate that an antibody or antigen binding fragment is expressed, thereby rendering moot the rejection of claims 35 and 62.

Finally, with respect to claim 60, it is believed that claim 60 is not ambiguous, as claim 61, which is dependent on claim 60, recites the second polynucleotide.

In light of these remarks, withdrawal of these rejections under 35 U.S.C. § 112, second paragraph, is believed to be in order and withdrawal is respectfully requested.

Interview

Applicants request an interview with the Examiner and her supervisor upon receipt of these papers.

Summary

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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